

[EDITORIAL]

Cholinesterase: Conflicting Aspects of Two Cardiovascular Diseases

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Cholinesterase is a family of esterases that dissolve choline-based esters and are synthesized only in the liver (1). The half-life of cholinesterase is shorter than that of albumin, which is 12 days (1). Since it is a functional marker of protein synthesis of the liver, the cholinesterase level can predict the outcome in patients with liver cirrhosis (1). In addition, the serum levels of cholinesterase be decreased under certain clinical conditions, such as inflammation, injury and infection, and malnutrition (1).

In patients with heart failure, decreased cholinesterase levels were reportedly associated with poor outcomes. Among 274 patients with heart failure with a preserved ejection fraction and mean age of 80 years old (2), the median level of cholinesterase was reported to be 208 U/L, and the lower tertile (≤ 180 U/L) was significantly associated with an increased risk of a composite endpoint of cardiovascular death and hospitalization for heart failure (2). Among 465 patients with chronic heart failure and a mean age of 62 years old (3), the median level of cholinesterase was 272 U/L, and patients with cardiac death and rehospitalization showed significantly lower cholinesterase levels than those without (239 vs. 292 U/L, $p < 0.0001$) (3). These two reports focus on the link between the decrease in serum cholinesterase levels and a poor outcome, along with other reports concerning cholinesterase and clinical conditions, such as inflammation and malignancy (1).

In this issue of *Internal Medicine*, Mito et al. reported the influence of high levels of serum cholinesterase on the presence of myocardial ischemia, as proven by invasive/non-invasive diagnostic modalities (4). They analyzed 559 patients suspected of having stable coronary artery disease without any history of cardiovascular disease and who had undergone coronary angiography. The patients were divided into four groups according to the serum cholinesterase quartile [low (< 234 IU/L), low-normal (234 to < 292 IU/L), high-normal (292 to < 345 IU/L), and high (≥ 345 IU/L) groups].

The mean age of patients was relatively young, and the prevalence of dyslipidemia, triglycerides levels, and body mass index increased with increasing quartile. The prevalence of myocardial ischemia also increased with increasing quartile, which was consistent with the increased prevalence of multivessel disease.

Even after adjusting for confounders, including the sex, age, body mass index, and other nutritional factors, the serum cholinesterase level remained significantly associated with the presence of myocardial ischemia. These results are very interesting and contain important information for clinicians. Apparent high cholinesterase is a marker of a high risk of atherosclerotic cardiovascular disease. The cholinesterase level can be increased under several conditions, including fatty liver, diabetes, and obesity (1, 5). The profiles of the patients in the higher quartiles established by Mito et al. suggested that the patients in higher quartiles might have metabolic disorders with higher body mass index (6), but some of the metabolic disorders such as diabetes and fatty liver, which might be reported by attending physicians, were not significantly different across quartiles (4). This implies that abnormally high cholinesterase levels may reflect the accumulation of visceral fat or an over-nutritional state beyond the acknowledged baseline characteristics (5, 6), which can lead to atherosclerotic cardiovascular disease.

The implications of low and high cholinesterase levels may differ between patients with heart failure and those with atherosclerotic cardiovascular disease. This conflicting aspect of cholinesterase may reflect disease progression from the accumulation of risks to the development of atherosclerotic cardiovascular disease and, finally, to heart failure. When we encounter patients with chest pain without any cardiovascular disease, we should carefully check their cholinesterase levels, and in patients with heart failure, low cholinesterase values may be an alarming sign.

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Of course, there are several limitations associated with Mito's study; for example, it includes no data regarding the long-term outcomes. In addition, an intervention or optimal medical treatment for the detected myocardial ischemia may alter the prognosis. Second, the cause-effect relationship is unclear given the cross-sectional nature of the study, as the authors stated (4). However, despite these limitations, the importance of this study is not hampered; it may shed light on the negative effects of a high cholinesterase level. Further research will be necessary to conclude the prognostic implication of high cholinesterase levels in patients with atherosclerosis or cardiovascular risks.

The author states that he has no Conflict of Interest (COI).

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